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The Eradication of Smallpox

A 10-year campaign led by the World Health Organization is right now at the point of success. The world may have seen its last case of the most devastating disease in human history

by Donald A. Henderson

Smallpox, the most devastating and feared pestilence in human history, is making its last stand in two remote areas of Ethiopia, one in the desert and one in the mountains. As of the end of August only five villages had experienced cases in the preceding eight weeks. More important, the onset of the last known case was on August 9. Because man is the only known reservoir for the smallpox virus, the disease should be eliminated forever when the last infected person recovers. Right now more than 1,000 Ethiopian health workers, together with 10 epidemiologists of the World Health Organization, are combing the countryside to make sure no more cases exist. If they discover one, the victim will be isolated under 24-hour guard and everyone who has been in contact with him will be vaccinated. An effort will be made to trace the chain of infection back to a previously known, contained outbreak. For two years after the last case is recorded the search will continue for additional outbreaks. If none is found, and if a WHO international commission can be satisfied that the search has been thorough, smallpox will be declared to have been eradicated from the earth. It will be the first such achievement in medical history.

The interruption of smallpox trans-

SEARCH FOR SMALLPOX CASES is pressed in the remote Simyen mountains of Ethiopia's Begemdir Province. Two-man teams are assigned to cover an area on foot or on muleback, looking for new cases and vaccinating any possible contacts. Supervisory personnel (in this case a World Health Organization epidemiologist and his Ethiopian counterpart) maintain contact with the teams by helicopter.

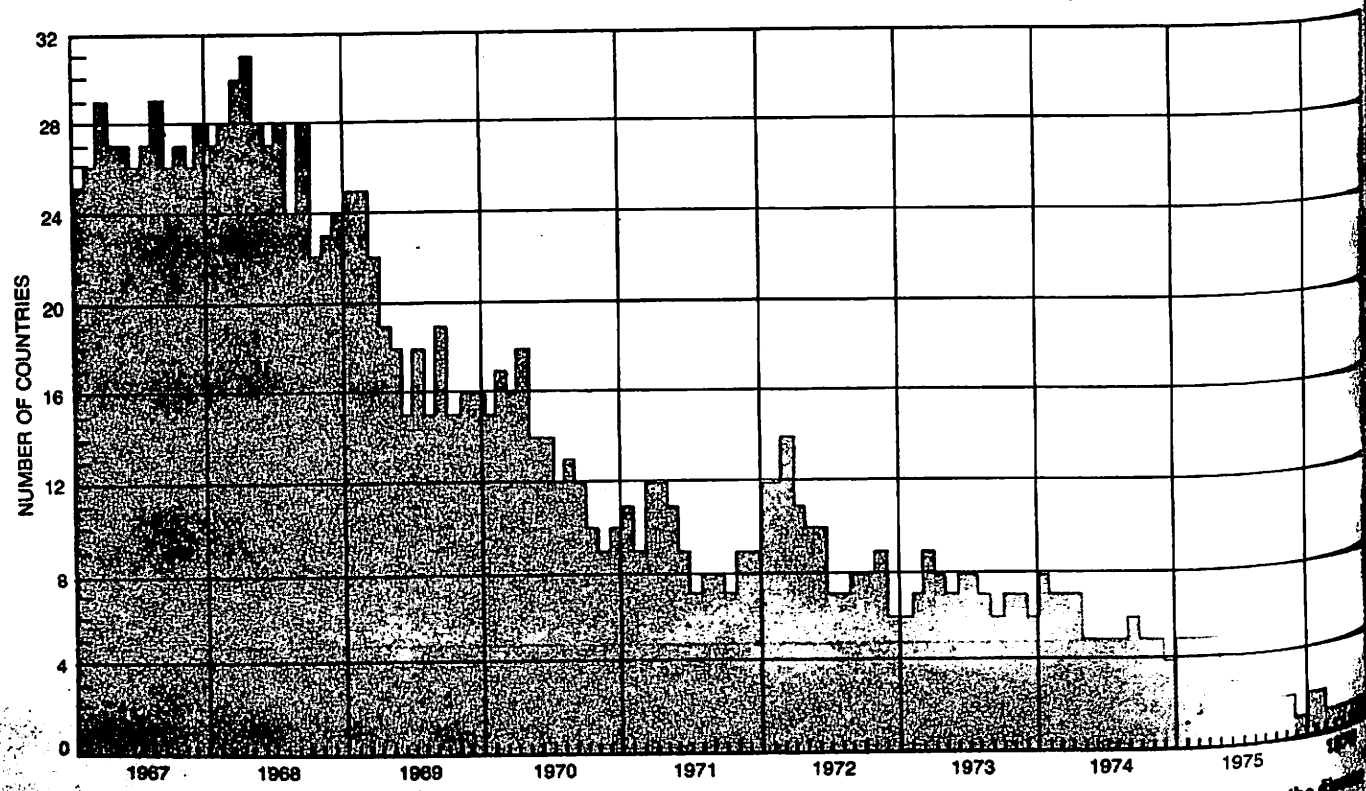
mission in 1976 was the objective of a 10-year global campaign voted by the World Health Assembly (the WHO's controlling body) in 1966 and launched in 1967. When the campaign began, smallpox was considered to be endemic—an indigenous, ever present illness—in more than 30 countries, and "imported" cases were regularly reported every year in perhaps a dozen other countries. The program moved forward steadily, with major campaigns eliminating smallpox successively in western and central Africa, Brazil, Indonesia, southern Africa, Pakistan, India and Bangladesh. In Ethiopia, the last infected country, the campaign has been complicated by some of the most rugged and inaccessible terrain in Africa; it is estimated that more than half of the country's 28 million people live more than a day's walk from any road. Fighting between government forces and various dissident groups has been a recurrent problem. Two Ethiopian health workers have been shot and killed, and the search teams have had to withdraw from some districts for weeks at a time. Yet ever since 1971, when the Ethiopian campaign began, both the extent of the infected areas and the number of cases have been steadily reduced, and now final success seems to be within reach.

Smallpox is caused by a virus that spreads from person to person in minute droplets discharged from the mouth or the nose. (Virus particles in clothing or bedding have sometimes infected people who have not had face-to-face contact with a patient, but such indirect infection has been infrequent.) About 10 or 12 days after inhaling the virus the infected person becomes sick, with a high fever and aching sensations resembling those of acute influenza. After two to four days a rash develops on the face, and within a day or two it spreads over the entire body. Usually it has a "centrifugal" distribution: it is densest on the face, arms and legs and less dense on the trunk. The small, red, pimplelike papules quickly become enlarged vesicles filled first with a clear serum and then, by the fifth day of the rash, with pus. In severe cases the pustules may be so close together, particularly on the face and eyelids, that there is no normal skin; the face is swollen and the patient, now acutely ill, may be unrecognizable. By the 10th day scabs begin to form, and by the third week they fall off, leaving depigmented areas that become pitted, disfiguring scars. Some patients are left blind. Among those afflicted by the virulent Asian form of the virus, variola major, from 20 to 40 percent die. In Ethiopia, where the less virulent variola minor is prevalent, the death rate is 1 percent. Once smallpox has been contracted there is no effective treatment for it.

The origin of smallpox antedates written history. The mummified head of the Egyptian pharaoh Ramses V, who died about 1160 B.C. of an acute infection, shows lesions that appear to be those of smallpox. Chinese and Sanskrit texts indicate that smallpox was also present at least that early in China and India. On the other hand, there is no mention of a disease resembling smallpox in either the Old Testament or the New or in Greek or Roman literature, and it would seem that such a serious disease would almost certainly have been described if it had been prevalent.

A plausible explanation lies in the same epidemiological characteristics of smallpox that lead us to believe it can now be eliminated. Since there is no known animal or insect reservoir of the virus, for infection to persist in a population one afflicted person must transmit the virus to a susceptible contact, and that contact in turn must transmit it to another in an unbroken chain. The smallpox victim can transmit the disease only from the time his rash appears until the scabs drop off, a period of about four weeks. After that he is immune to reinfection. In isolated villages and among scattered populations a point is therefore reached where so few people remain susceptible that the chain of transmission is broken. In such an area smallpox dies out, and it does not recur unless it is reintroduced.

It seems reasonable to speculate that in ancient times only the more densely populated areas of India and China

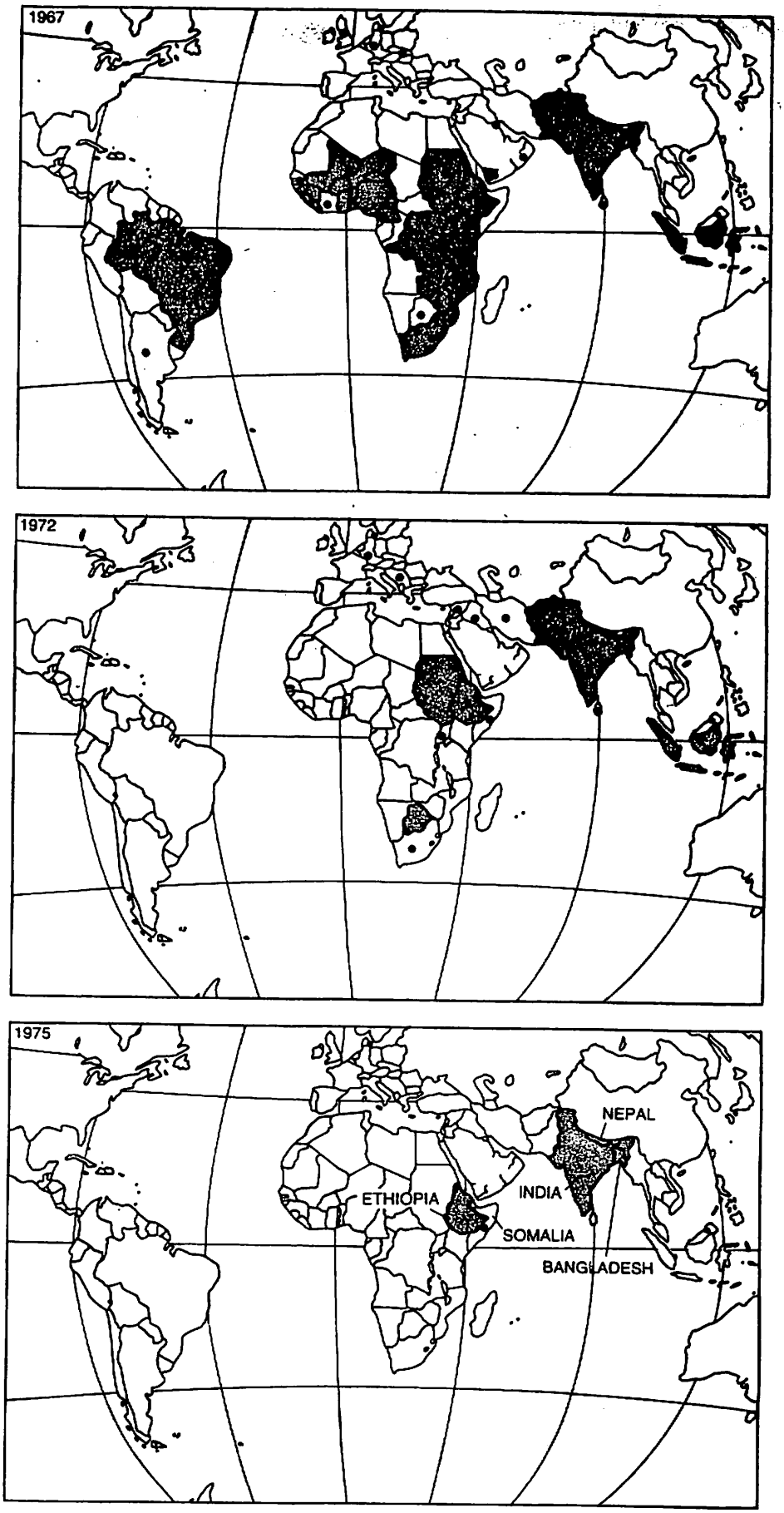


TEN-YEAR TREND in the incidence of smallpox is traced here by a histogram showing the number of countries reporting one case or more each month. That includes cases in countries where the disease was endemic and also cases "imported" into nonendemic countries.

were able to sustain the continued transmission of smallpox. If it was occasionally introduced into less populated central and western Asia, Europe and Africa, it might have persisted for a time in such a region as the Nile delta, but eventually the chain of transmission would have been broken. The slow pace of travel in pre-Christian times and the infrequency of long journeys could have served to confine smallpox largely to Asia during that period. In the early Christian Era, however, descriptions of a disease that was almost certainly smallpox appear increasingly in historical accounts of western Asia and, beginning in the sixth century, of Europe and Africa. In 1520 Spanish conquistadors brought the disease to the Americas.

Increasing population densities provided enough susceptible individuals to sustain the chain of transmission. So pervasive was the disease that, like measles in our time, virtually everyone contracted it. English parish records of the early 18th century indicate that about 20 percent of all smallpox victims died but that the rate was higher in many epidemics. In one well-documented instance in Iceland in 1707, 18,000 people, or 31 percent of a population of 57,000, died of smallpox. Since part of the population was immune because of previous smallpox, the death rate in that epidemic may have approached 50 percent. In Mexico 3.5 million indigenous people are believed to have died of smallpox shortly after it was introduced in the 16th century. Until the advent of vaccination smallpox played a major role in inhibiting population growth.

Even before Edward Jenner's day some people had been protected against smallpox by variolation: material from the pustules of a patient was scratched into the skin of a healthy person, who, if all went well, developed a mild case and was subsequently immune [see "The Prevention of Smallpox before Jenner," by William L. Langer; SCIENTIFIC AMERICAN, January]. Variolation spread from Asia via the Near East into Europe as a folk practice, and in the early 18th century it was taken up and popularized by physicians in England. The death rate from variolation was only about a tenth as high as the mortality from the naturally acquired disease, but a variolated person could transmit virulent smallpox to others. (Recent outbreaks in Ethiopia have been traced to the practice.) When variolation became widespread in England, it was common knowledge that dairymaids who had contracted the illness called cowpox would not "take the smallpox" when they were variolated and also appeared to be immune to natural smallpox infection. In 1796 Jenner inoculated material from a dairymaid's

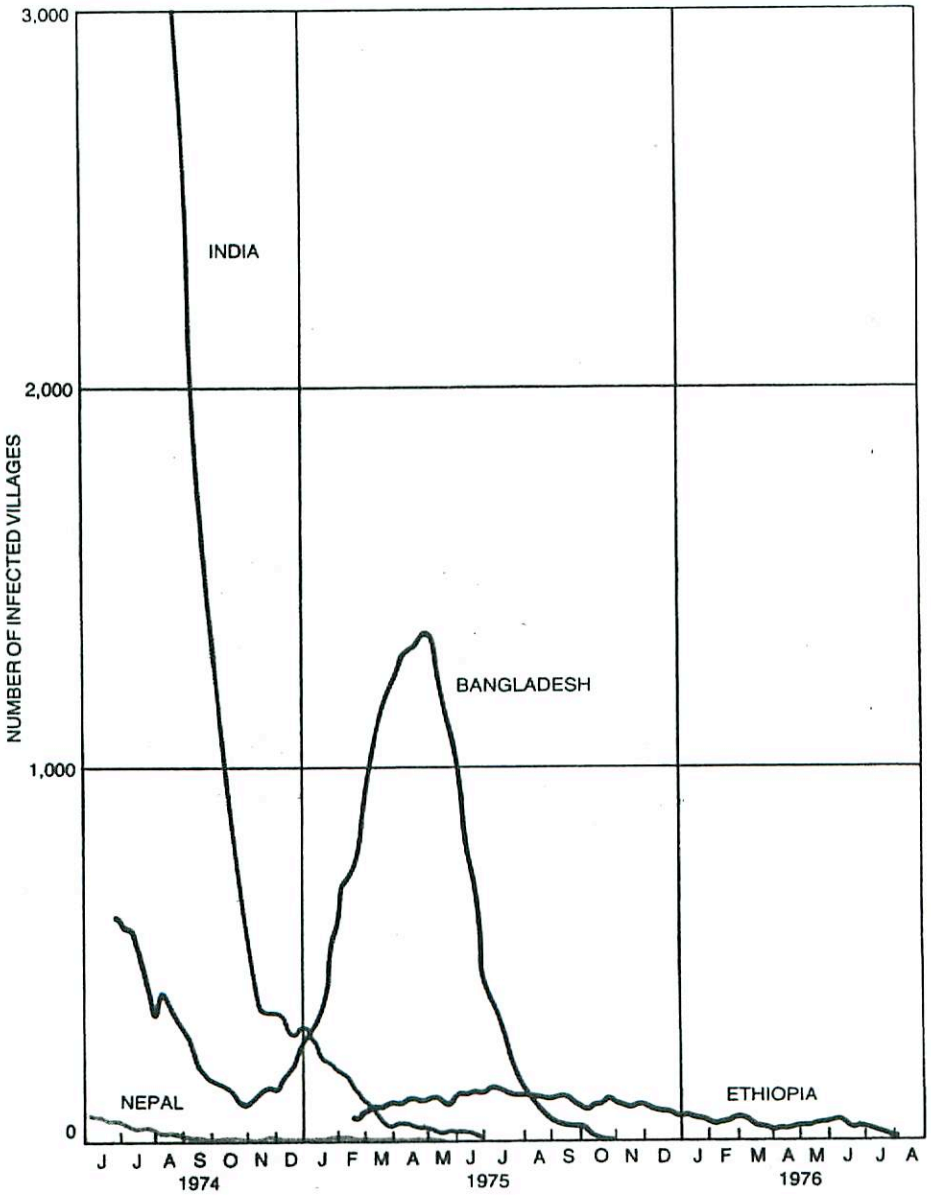


AREA AFFLICTED BY SMALLPOX has shrunk as shown on maps for 1967 (*top*), 1972 (*middle*) and 1975 (*bottom*). The countries where the disease was considered endemic, or indigenous, are shaded in color; those reporting imported cases are designated by a colored dot.

cowpox lesion into the arm of an eight-year-old boy, who was subsequently immune to the effects of smallpox variolation. Jenner called the new procedure vaccination, and he predicted that "the annihilation of smallpox must be the final result of this practice." The new technique spread rapidly, but it is only now, as the result of a concerted international public-health effort, that Jenner's prediction is being fulfilled.

Until late in the 19th century virus for vaccination was obtained from the pustular lesion of one vaccinated person and was scratched into the arm of other individuals to be vaccinated. It was an inefficient system, and not infrequently the syphilis spirochete and hepatitis virus were transferred along with the vaccine virus. The discovery that large amounts of vaccine virus could be obtained by scarifying and inoculating the shaved flank of a calf was an important advance. (That procedure is still followed to obtain sufficient quantities of virus for vaccine production.) Preservation of the virus was difficult, however, particularly in tropical climates. Sometimes the calf was led from door to door and a bit of pus was scraped from its flank for each vaccination, but usually the pustular material scraped from the calf was suspended in a 50 percent solution of glycerol in order to reduce bacterial contamination and was distributed in small glass capillaries. In this form and without refrigeration the vaccine remained potent for perhaps a few days.

Jenner himself had noted that dried vaccine lasted longer than liquid vaccine, but for years there was no way to produce dried vaccine in bulk. Methods for the commercial freeze-drying of biological preparations were developed just before World War II, and in the early 1950's a technique for producing a remarkably heat-stable freeze-dried smallpox vaccine was devised by Leslie H. Collier of the Lister Institute in England. Instead of drying the crude pulp scraped from the animal, Collier produced a partly purified suspension of virus by differential centrifugation and freeze-dried the material in the ampules in which it was to be distributed. It was reconstituted with a glycerol solution for the vaccination. Most batches of Collier's vaccine were still potent after storage for two years at body temperature. Potent dried vaccine was an essential tool that could make the eradication of smallpox possible.



FINAL STAGES of eradication campaigns in the last four endemic countries have been monitored by a weekly count of "infected villages," defined as those reporting a case within the past six weeks. The countdown was instituted in Ethiopia only early in 1975 and it was not until the summer of that year that it was considered to represent a reasonably complete national total.

In 1926, when the Health Section of the League of Nations began publishing a weekly bulletin on disease prevalence around the world, smallpox was made a reportable disease, but only against opposition. When a Japanese delegate to the International Sanitary Conference suggested that smallpox be made reportable, a Swiss delegate maintained that "smallpox has, in reality, no place in an international convention. It is not a pestilential disease in the proper sense of the term; it is, in effect, a disease that exists everywhere. There is probably not a single country of which it can be said that there are no cases of smallpox."

When the WHO was established in 1948 as a specialized agency of the United Nations, it approached the smallpox problem gingerly at first; its interim commission had stated in 1946 that it was "impracticable as yet" even to standardize smallpox vaccines. By the late 1940's, however, the concept of disease eradication in general and the idea of eradicating smallpox in particular were acquiring a growing number of supporters, one of the most persuasive being Fred L. Soper, director of what was then the Pan American Sanitary Bureau and is now the WHO Regional Office for the Americas. They pointed to the very practical demonstration of the elimination of smallpox from North America and Europe in the 1940's and also to a more notable achievement—from a few countries with less highly developed health services, such as the Philippines and some countries in Central America. A campaign to eradicate smallpox in the Americas was undertaken in 1950, with the Pan American Sanitary Bureau providing technical assistance. The results were encouraging: by 1959 smallpox had been effectively eliminated from all American countries except Argentina, Brazil, Colombia, Ecuador and Haiti.

In that year, on the initiative of the U.S.S.R., the World Health Assembly called for global smallpox eradication and vaccination "*in foci* where the disease exists." The resolution [illegible]

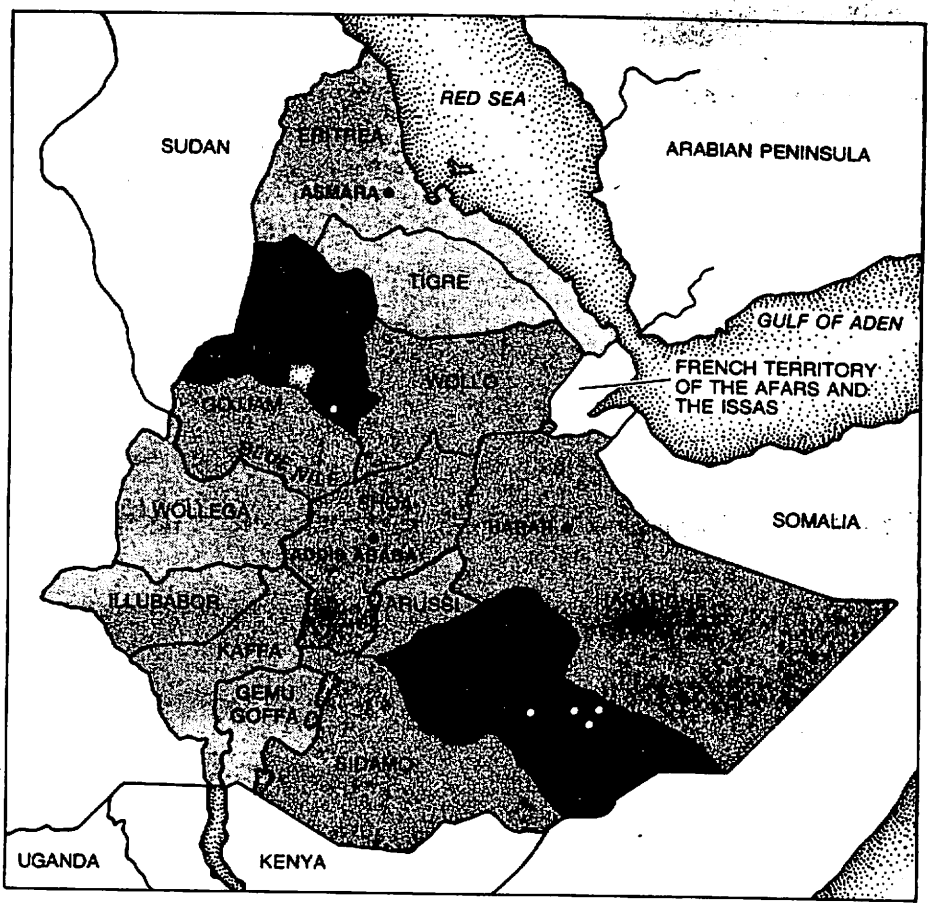
out that "funds devoted to the control of and vaccination against smallpox throughout the world exceed those necessary for the eradication of smallpox in its endemic foci."

The WHO and the UN Children's Fund (UNICEF) helped a number of countries to establish vaccine-production centers. Donations of vaccine were received from several countries, and mass-vaccination programs were started by some. Progress was slow, however. A global program to wipe out malaria had captured the interest and energies of some governments and health workers, and when it faltered, many came to doubt the feasibility of any disease-eradication program. Lack of skilled personnel, vehicles and other necessary assistance kept many countries from undertaking campaigns. Those that did make the attempt were often beset by cases of smallpox imported from adjacent countries. Vaccine donations were far too small to meet the need, and there was no mechanism for regular monitoring of the quality of vaccine produced in newly established production centers. Vaccine quality declined, and countries that found themselves administering poor vaccines became disillusioned.

In 1966 delegates to the World Health Assembly argued that either enough money should be provided for a fully coordinated program or the idea of global smallpox eradication should be given up. After lengthy debate and in spite of many misgivings the delegates voted a special budget of $2.5 million for an intensive program to begin on January 1, 1967. The objective was to eliminate smallpox from the world by the end of 1976.

In 1967, the year the intensified eradication program began, smallpox was considered to be endemic in 33 countries, and 11 others reported cases attributable to importations. In the Americas, Brazil was the only endemic country, but it alone constituted half a continent. In the rest of the world there were three major reservoirs of smallpox. One, in Asia, extended from what is now Bangladesh through India, Nepal and Pakistan into Afghanistan. A second reservoir comprised virtually all of Africa south of the Sahara. The third reservoir was the Indonesian archipelago.

At the start of the program the urgent need was for adequate supplies of potent and stable freeze-dried vaccine. Little satisfactory freeze-dried vaccine was being produced anywhere. Some vaccines lacked potency when they were reconstituted and others quickly lost their potency under field conditions; some that were being administered contained no detectable virus whatever. Almost no vaccine in the endemic countries met the WHO's basic standards, and there was no central laboratory for testing vaccines.



IN ETHIOPIA all 14 provinces were infected with smallpox in 1971, when the WHO-directed eradication program began. At the end of 1974 seven provinces (*medium and dark color*) still remained infected. At the end of August this year there were infected villages (*white dots*) in only two provinces (*dark color*), in the gorge of the Blue Nile and in the Ogaden Desert.

At the WHO's request two major laboratories agreed early in the campaign to serve as international vaccine reference centers: the Rijksinstituut voor de Volksgezondheid in the Netherlands and Connaught Laboratories, Ltd., of Toronto. It was estimated that 250 million doses of vaccine a year would be needed for the endemic areas. Buying that amount would have cost more money than had been set aside for the entire program, and so a decision was made not to buy any vaccine but to ask for donations of it, and to provide equipment and technical advice to laboratories within the endemic regions so that at least the most populous endemic countries could produce good vaccine on their own.

In the first years most of the vaccine—more than 140 million doses a year—was given by the U.S.S.R. and 40 million doses came from the U.S. Eventually donations were received from more than 20 countries. Gradually vaccine production in the developing countries increased and the quality improved, until by 1970 all the vaccine in the program met accepted international standards of potency and stability.

Another problem was how to simplify and improve the vaccination techniques. The commonest technique throughout the world when the program began was some form of the scratch method: a drop of vaccine was placed on the skin and scratched into the superficial layers, sometimes with instruments that made severe wounds. The technique was wasteful of vaccine and achieved a lower success rate than an alternative method in which a needle is held parallel to the skin and the tip is pressed into the skin repeatedly. This multiple-pressure procedure is difficult to follow and to teach, however. A more efficient method that consumed less vaccine was needed.

A jet injector, originally designed for a deeper, subcutaneous injection but modified to accomplish the more superficial smallpox vaccination, had been developed by the U.S. Army. Under high pressure it injected a tenth of a milliliter of vaccine into the superficial layers of the skin. The gun required a more highly purified vaccine than the scratch methods but less than a third as much virus, and more than 1,000 people an hour could be vaccinated with the gun (if that many could be gathered together). Introduced in 1967 for programs in

western and central Africa assisted by the U.S. Center for Disease Control, the jet guns proved to be effective, but they were expensive and required considerable maintenance and repair, making them impractical in places where trained technicians were unavailable. And they were of limited benefit in Asia, where vaccination traditionally was done on a house-to-house basis.

The ultimate solution, the bifurcated needle, was developed at Wyeth Laboratories in the 1960's. It resembles a large, blunt sewing needle with part of the eye ground off to leave two small prongs. The bifurcated end of the needle is dipped into the vaccine, and one drop, enough for one vaccination, clings between the prongs. The needle is held perpendicular to the skin and 15 quick punctures are made. Only one-fourth as much vaccine is required as for the scratch technique. Wyeth waived patent charges for the design for any manufacturer producing the needles exclusively for the WHO program. The needle had originally been designed to be used once, but the WHO had them made of special steel so that they could be boiled or flamed more than 200 times without becoming dull.

Vaccination technique was further simplified after field studies revealed that there was no difference in the incidence of bacterial infections whether or not the vaccination site had first been swabbed with acetone, alcohol or soap. That made it possible to dispense with cotton swabs and bottles of soap and alcohol. The vaccinator needs only a vial of diluent for the vaccine, a container of sterile needles and another container for used needles, all of which fit handily into a shirt pocket.

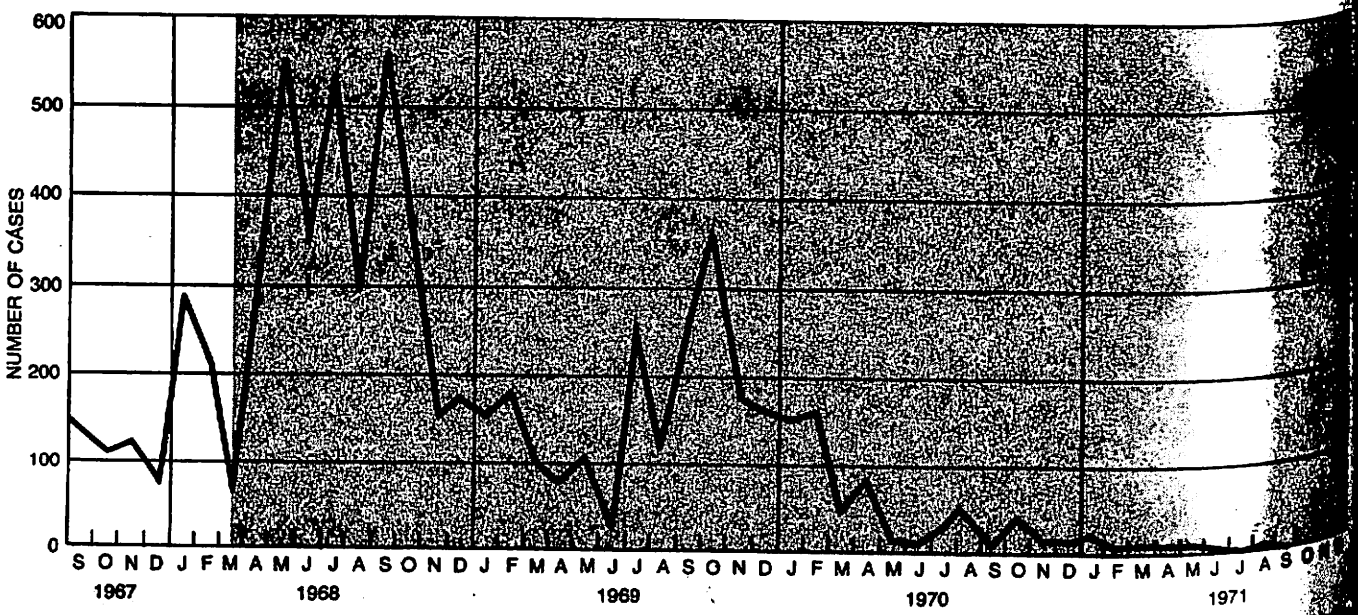
At the beginning of the program there were heavily endemic areas, but it was not at all clear how prevalent the disease was, or how extensive. It quickly became apparent that routine reporting of smallpox cases, particularly in the endemic parts of the world, was far worse than had been supposed; it was so bad that for certain years some large areas were reported as having more smallpox deaths than they had cases. One study in northern Nigeria indicated that the efficiency of reporting was 8.1 percent in an urban area and 1.3 percent in rural areas; in West Java it appeared that not more than 6 percent of all cases had been reported. In the light of nine years of experience we now believe that when the program began not more than 1 percent of all cases were actually being reported. Although 131,418 cases of smallpox worldwide were reported to the WHO in 1967, there may have been that many cases in northern Nigeria alone. An accurate figure for the world in 1967 might be on the order of 10 to 15 million cases.

A major problem was that even when cases were detected and reported by health units they were not necessarily included in national reports. At the time the campaign began in Indonesia only about half of the cases reported at the provincial level were being reported nationally; in Niger, of 325 cases reported to local government units between December, 1966, and February, 1967, only 14 were finally reported to the ministry of health. A first step in national smallpox-eradication campaigns was therefore to increase the quality and regularity of reporting from all fixed medical units. One approach was to appoint a surveillance team of two to four people for each administrative division with two to five million in population. These teams circulated among the medical units encouraging them to report, looking for cases, distributing vaccine, counseling and cajoling.

When the intensified eradication program began, the basic strategy called for a two- to three-year mass-vaccination campaign throughout a country, during which an improved reporting and surveillance system would be developed. It was felt that if 80 percent of the population could be vaccinated, smallpox incidence would be reduced to fewer than five cases per 100,000 of population thereafter, with improved surveillance the remaining foci would be identified quickly and measures could be taken to eliminate them.

A development early in the campaign resulted in a change in that strategy. There was a delay in the delivery of supplies for the mass-vaccination program in eastern Nigeria, and an energetic U.S. adviser, William H. Foege, organized an interim program: he searched out smallpox cases and vaccinated thoroughly in a limited area surrounding each case [*see illustration on opposite page*]. The mass campaign supplies arrived only a few months later, but by then there was no detectable smallpox in eastern Nigeria. And less than half of the population had ever been vaccinated.

This result and similar experiences in other places led to an emphasis, even in the early stage of the campaigns, on what became known as surveillance-containment: improved search and detection as speedily as possible, isolation of patients and vaccination of every known or suspected contact around



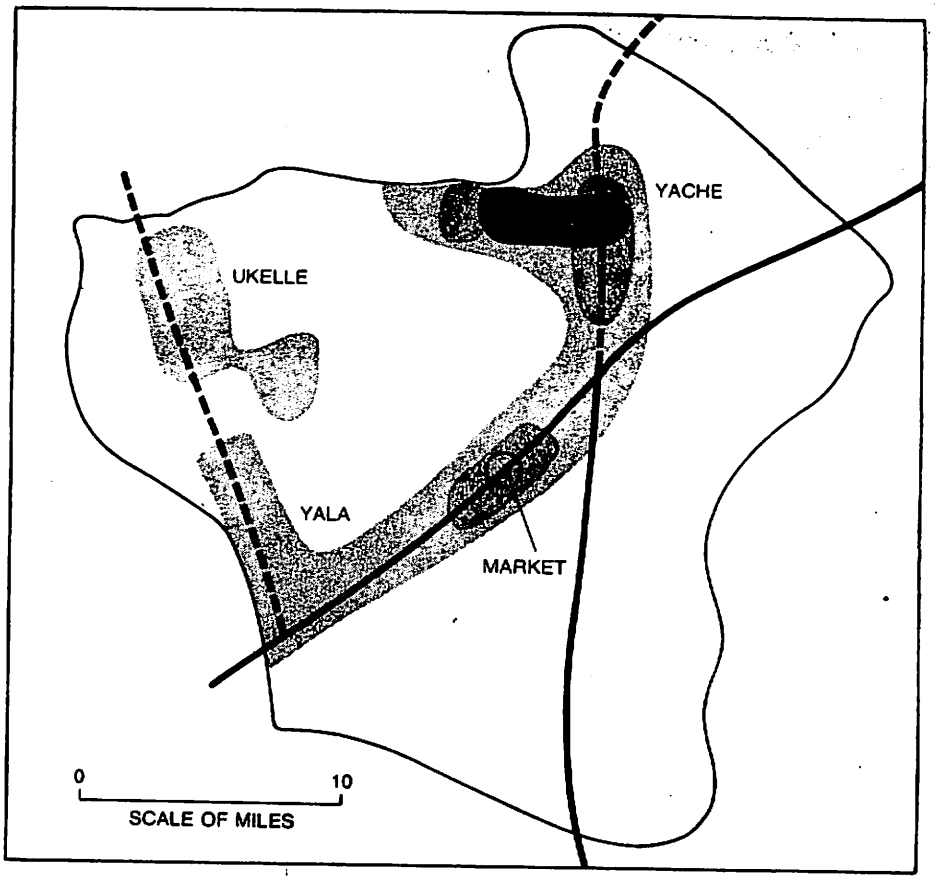
IN ZAÏRE (then known as the Democratic Republic of the Congo) an intensified eradication program began in March, 1968. The curve of reported smallpox cases is typical: as the program got under way improved reporting produced what appeared to be an increased incidence of smallpox. After six months a fairly steady but low decline began, and the last case was recorded during August

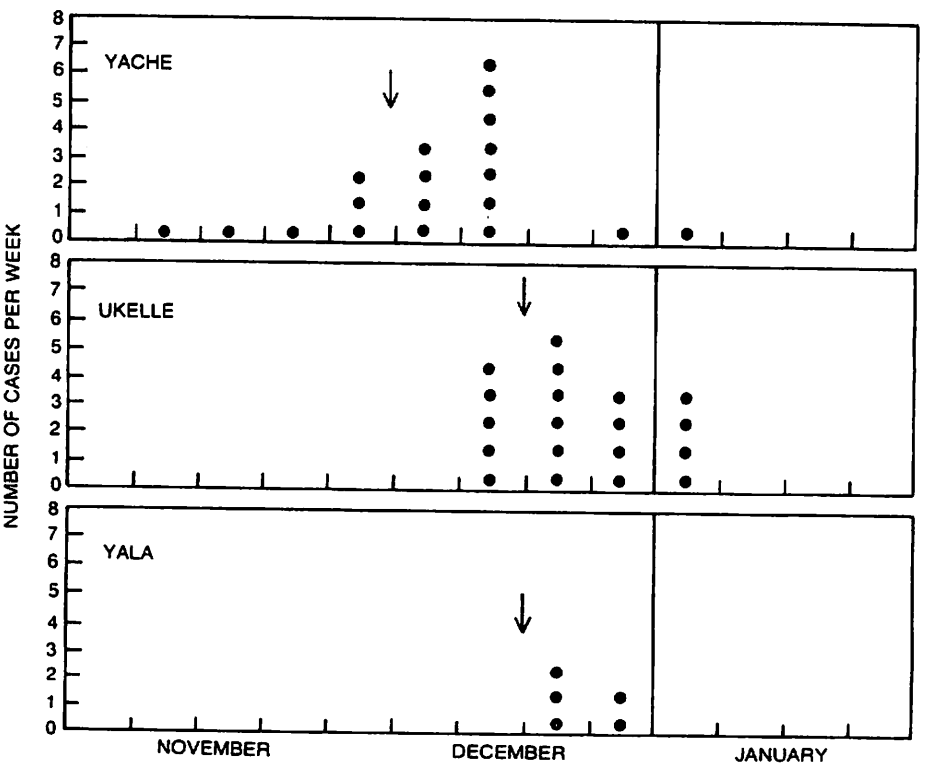
them. The procedure sealed off outbreaks from the rest of the population. That proved to be effective partly because in most areas smallpox turned out to spread slower than had been supposed. One person generally infected no more than two to five others; cases were usually clustered in one part of a town or in adjacent villages rather than being widely and evenly distributed through a country. The containment teams could focus on problem areas and had somewhat more time than had been anticipated in which to seal off an outbreak. When it became clear that smallpox in a previously vaccinated person was uncommon even if the vaccination had been done many years before, heavy emphasis was placed on primary vaccination. (In Asia 80 percent of all cases were reported among the 20 percent of the people who had no vaccination scar.)

Substantial progress was made in the four years after 1967. In 1971 only 16 countries reported smallpox cases. In the 20 countries of western and central Africa where the U.S. Center for Disease Control was providing support the last case was recorded (in Nigeria) in June, 1970, a full year earlier than had been expected. Elsewhere in Africa endemic smallpox was limited to Ethiopia, whose program did not begin until 1971, to the southern Sudan, where civil war had made a program impossible, and to Botswana, which had been reinfected at about the time of the last cases in neighboring South Africa. Brazil's last case developed in April, 1971, and Indonesia's in January, 1972. One major reservoir of smallpox remained, and it was n Asia.

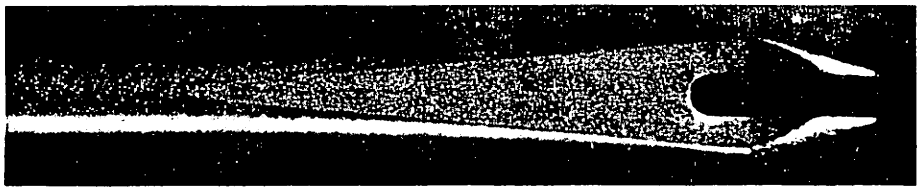
In 1972 an extensive area still heavily endemic with smallpox stretched from Bangladesh through northern India and Nepal into Pakistan. Here case detection was inadequate and reporting systems were archaic; the importance of surveillance and containment was not appreciated, and when containment was attempted, it was usually done poorly. Support for the program by health authorities was lukewarm; so many efforts to control smallpox had failed over so many years that the disease was widely considered inevitable and its elimination impossible.

During the 1972–1973 smallpox season in India a WHO epidemiologist, tracing the source of infection of a case in the southern state of Andhra Pradesh, followed the trail into an adjacent state that was thought to be smallpox-free. There in one district he discovered a major epidemic. It had been known to district health workers but had been concealed. Rapid containment was crucial, but that required the prompt detection of all cases throughout a district of two





OUTBREAK IN NIGERIA at the outset of the campaign was dealt with by containment, which proved so effective that it later largely replaced mass immunization in Asia. The outbreak was reported on December 4, 1966, in Yache, a village in the Ogoja district (*map at top*). Vaccination began that day in the area (*dark color*) immediately surrounding the known cases and was extended, as new cases were reported, to successively implicated areas (*medium color and light color*). The table (*bottom*) relates cases by week of onset to the initiation of vaccination. In each village the outbreak was ended within two or three weeks after vaccination began (*arrows*), except for two individuals in Yache who were not successfully immunized. The experience demonstrated that an outbreak could be extinguished by vaccinating people in a limited area around each new case even if the general area contained many unvaccinated people.



BIFURCATED NEEDLE was the principal tool of the vaccination program. The simple instrument was developed by Wyeth Laboratories. The pronged end of the needle is enlarged about 10 diameters in this photograph; the actual length of the needle is about two inches.

million people. All available health personnel were mobilized for a house-to-house search, which was two weeks in preparation and one week in execution. It revealed numerous previously undisclosed cases in addition to those recently discovered. Containment vaccination around each outbreak eliminated smallpox from the district within weeks. The experience underscored the danger of poor reporting, but it also showed what could be gained by a thorough search and demonstrated that vast numbers of health workers were deployed in India and could be mobilized quickly. Plans were made to undertake the same kind of search throughout India.

In October, 1973, the smallpox-eradication program in India conducted the first of a series of week-long searches that were scheduled once a month and involved more than 100,000 health workers. The results of the first search were ominous. The state of Uttar Pradesh, with a population of 90 million, had regularly been reporting from 100 to 300 cases of smallpox per week. The first one-week search in the state found more than 7,000 cases. And that was not all: a later assessment showed that only half of the villages officially reported as having been searched had actually been visited.

After that the techniques of case search were steadily improved. Between search weeks special surveillance teams asked questions at markets and in schools to uncover rumors of cases. A reward was offered to anyone who reported a case of smallpox and to the health worker receiving the report. As the incidence of smallpox declined the amount of the reward was increased, always with extensive publicity. Containment measures were tightened. Special books were prepared in which every person in an infected village and for one mile around it was listed. Guards hired locally were stationed day and night at the homes of smallpox patients to keep the patient from leaving and to see to it that all visitors were vaccinated.

As case detection and notification improved, the number of reported cases climbed steeply. More than 218,000 cases were reported in India in 1974, the highest total recorded since 1958. Some newspapers called it a disaster, and more than one wrote an obituary of the global eradication program. Those involved in the program, however, felt that in the search tactic they had at last the key to smallpox eradication on the subcontinent.

In June, 1974, a new unit of measurement was adopted: the "infected village." A village (or a ward in a city) was listed as infected if even one case was reported there; it remained on the list until six weeks after the onset of the last case and until an epidemiologist had certified (after a special search) that transmission had been stopped. The epidemic in India peaked in July, 1974, at which time there were more than 7,000 infected villages. The number fell steadily until in November it reached 350 but then the decline stopped. This caused concern because a new post-monsoon season with more rapid transmission of infection was beginning. Additional epidemiologists joined the fight, containment was made more rigid and in January the incidence of smallpox again began to decrease. May 24, 1975, saw the onset of the last known case of smallpox in India.

Afghanistan had become smallpox-free in 1972, and Pakistan's last case was in October, 1974. Nepal, plagued by importations from India, recorded its last case in April, 1975. Bangladesh proved to be more difficult. There was great optimism late in 1974, when the number of infected villages in the country declined to only 91. Unfortunately nearly all of the infected areas were in a region struck by famine after the most devastating flood in decades. Thousands of infected refugees began moving through Bangladesh, and in spite of heroic efforts it was impossible to stem the spread of disease. (In two days in one marketplace one beggar infected 52 people from 18 villages.) A further blow came in January of 1975, when slums in Dacca, the capital city, were bulldozed and about 500,000 people were displaced. Many of these people, some of them infected with smallpox, fanned out through the country, producing dozens of satellite outbreaks; the number of infected villages rose to a peak of 1,208 in April. Then, under a presidential directive, a national emergency program was launched and the number of infected villages decreased sharply and steadily. On October 16, 1975, the occurrence of the last case in Bangladesh was reported. The patient, three-year-old Rahima Banu, was the world's last known victim of the severe form of smallpox.

REWARD FOR REPORTING a smallpox case is announced by a wall poster in Bangladesh. The Bengali writing offers a "250-taka prize" (about $17) to anyone who reports a smallpox case to a health office. Reports and even rumors of cases were followed up by health workers.

TWO SMALLPOX PATIENTS, both in Bangladesh, are pictured with their mothers. In the severe case (*left*) the pustules are so closely spaced on the face that they touch one another; the rash is less dense on the trunk. The three-year-old girl recovering from smallpox (*right*) was the last known victim in Bangladesh and thus the world's last known case of the more virulent form of the disease, variola major.

major. After that 12,000 health workers supervised by nearly 100 epidemiologists repeatedly searched Bangladesh house by house. They found no cases, and it is unlikely that any more will be discovered, but surveillance will continue for two years.

There has been some concern that smallpox, after having been declared eradicated, might emerge again from an unknown animal reservoir, from dormant virus in old scabs or from some other source. The most impressive evidence against the likelihood of such recurrence is the fact that for nine years no cases of smallpox have been discovered in the vast areas that have been smallpox-free, except for those imported from known endemic areas. Although 30 cases of an illness closely resembling smallpox have been detected in regions of Africa declared smallpox-free, in each such case "monkeypox" virus has been isolated, or identified by antibodies in victims' blood serum, as the causative factor. The reservoir of monkeypox is not known, but it is probably among rodents rather than monkeys. The disease is related to smallpox but is caused by a different virus, and its capacity for spreading from one human being to another appears to be almost nil.

What of the cost of the 10-year campaign? Approximately $83 million has been spent in international assistance for the smallpox-eradication program since 1967. The endemic countries themselves have spent roughly twice that amount, but few of them have spent much more than they were already spending on smallpox control. The total amount of money spent in international assistance is little more than half what was computed in 1968 to be the yearly expenditure for smallpox control in the U.S. alone; worldwide expenditures for smallpox vaccination and quarantine measures have been estimated as being in the range of from $1 billion to $2 billion a year. With the eradication of the disease smallpox vaccination will no longer be required, nor will international certificates of smallpox vaccination. Apart from the alleviation of human suffering, the savings have already repaid the small investment many times over.

The eradication of smallpox will represent a major milestone in the history of medicine. It will have demonstrated what can be achieved when governments throughout the world join an international organization in a common purpose. In perspective, however, the campaign must be seen as representing only a small first step toward achieving a tolerable level of public health throughout the world.

A logical next step would be to apply what has been learned in this campaign to immunization programs for controlling diphtheria, whooping cough, tetanus, measles, poliomyelitis and tuberculosis. Effective vaccines are available for all these diseases, but there has been little immunization outside the developed world. Now a number of the developing countries, given the confidence of achievement and recognizing how much can be accomplished *with very little*, have embarked on new immunization programs. With such campaigns one begins to see a perceptible—although far from adequate—shift from curative medicine for the rich to preventive med-